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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/569,812	02/10/2006	Ian Holmes	PB60441	6556

20462 7590 04/05/2007

SMITHKLINE BEECHAM CORPORATION
CORPORATE INTELLECTUAL PROPERTY-US, UW2220
P. O. BOX 1539
KING OF PRUSSIA, PA 19406-0939

EXAMINER	
LAO, MARIALOUISA	
ART UNIT	**PAPER NUMBER**
1621	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/05/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/569,812	HOLMES ET AL.	
	Examiner	Art Unit	
	MLouisa Lao, Ph.D.	1621	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7,9 and 10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7 and 9* is/are rejected.

7)☒ Claim(s) *10* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/20/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Objections

1. **Claim 1 is objected** to because of the following informalities: counting from the bottom of page 4, lines 3-4, the applicants recite the butanedioic acid [3-methoxy-4-(phenylmethoxy) phenyl]; or butanedioic acid [4-(phenylmethoxy)phenyl]. It is suggested that these compounds be recited as [3-methoxy-4-(phenylmethoxy)phenyl]butanedioic acid or [4-(phenylmethoxy)phenyl] butanedioic acid.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. **Claim 7 is rejected** under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the method for the treatment of a human or animal *suffering from* an inflammatory disease or an autoimmune disorder comprising administering to said subject an effective amount of a compound of Formula I, as recited, does not reasonably provide enablement for method for the treatment of a human or animal *susceptible to* an inflammatory disease or an autoimmune disorder. The specification does not enable the person skilled in the art of clinical pharmacy, to make the invention commensurate in scope with these claims. The factors to be considered [in making an enablement rejection] have been summarized as a) the quantity of experimentation necessary, b) the amount of direction or guidance presented, c) the

presence or absence of working examples, d) the nature of the invention, e) the state of the prior art, f) the relative skill of those in the art, g) the predictability or unpredictability of the art, and, h) the breadth of the claims.

4. In the present case, the important factors leading to a conclusion of undue experimentation are the absence of any working example of a method for the treatment of a human or animal *suffering from* an inflammatory disease or an autoimmune disorder, the lack of predictability in the art, the amount of direction and guidance provided and the broad scope of the claim.

a) the amount of experimentation needed. Since the compounds of Formula I and Ia are replete with substituents effectuating to different structures with invariable distinct characteristics, the quantity of experiments corresponding thereto, would likewise be numerous.

b) the amount of direction and guidance provided. The specification on page 18 recites the possibility of testing the compounds of the invention in *in vitro* assays.

c) the presence or absence of working examples. There are no working examples of method for the treatment of a human or animal *susceptible to* an inflammatory disease or an autoimmune disorder. Claim 7 is drawn to "method for the treatment of a human or animal *suffering from* an inflammatory disease or an autoimmune disorder", yet the various examples presented are found deficient to encompass the population of humans and animals "prone" or "susceptible to" said disorders. Hence, the applicants are requested to show that the method for the treatment of a human or animal *suffering from* an inflammatory disease or an autoimmune disorder compound of formula I is applicable to the population *susceptible to* said disorders, or limit claim 7 accordingly.

d) the nature of the invention and the e) the state of the prior art. Compounds of the structure as recited in Formula (I) are known, see Muller et al. (US6380239, US'239).

f) the relative skill of those in the art. The skilled artisans are synthetic organic chemists and clinical pharmacists with graduate degrees and potentially with many years of research and industrial experience.

g) the predictability or unpredictability of the art. The state of the art of method of treatment is unpredictable, since this art is largely empirical, which requires fulfilling a rationale for the optimization of absorption, distribution, metabolism, and excretion of a drug. Determining whether a compound meets the attributes of a useful prodrug entails substantial clinical testing with laborious experimentation. See Goodman & Gilman's *The Pharmacological Basis of Therapeutics".* 10th ed. NY McGraw Hill 2001 p3.

h) the breadth of the claim. Claim 7 is recites method for the treatment of a human or animal *suffering from* or *susceptible to* an inflammatory disease or an autoimmune disorder comprising administering to said subject an effective amount of a compound of Formula I. This is broad. Further, it is unclear whether the applicants intend to encompass the entire population of either humans or animals, since "susceptibility" entails *all* populations and may be interpreted to mean "prevention".

5. MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/use the full scope of the claimed invention without undue experimentation. In re Wright 999 F.2d 1557,1562, 27 USPQ2d

1510, 1513 (Fed.Cir.1993)." That conclusion is clearly justified here. Thus, undue experimentation will be required to practice Applicants' invention.

Claim Rejections - 35 USC § 102

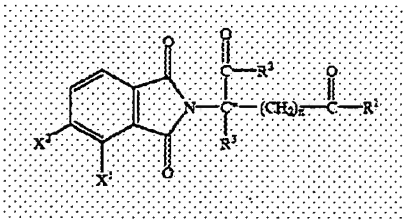
6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. **Claims 1-5, 7 and 9 are rejected** under 35 U.S.C. 102(b) as being anticipated by Muller et al. (US6380239, US`239).

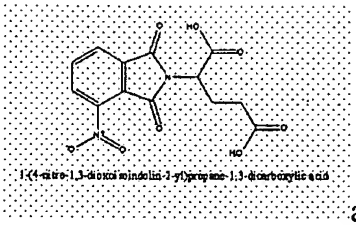
8. The instant claims are drawn to the compounds of Formula (I), Formula (Ia), a method for, *inter alia,* the treatment of inflammatory disease and a pharmaceutical composition comprising said compounds of Formula (I).

9. US`239 teaches in columns 21-22 claims 1-4 and 6-9 the compounds of the formula



and corresponding examples thereto.

10. US`239 anticipates the instant claims when R^1= optionally substituted $-C_{2-10}$alkylcycloalkyl, Z= is a bond, Q= optionally substituted 5-membered heteroaryl, R^2= $CONH_2$ and X=COR^3 where R^3=OR^6 and R^6=H and/or R^3=NR^8R^9, where R^8 and R^9 are H. Illustratively,

the following compound  anticipates the instant claims of the compounds, as recited.

11. Further, US`239 recites in claims 5-8 column 21 that the aforementioned compounds are used in a method of treating a mammal of *inter alia,* inflammatory bowel disease. US`239 also recites in claim 9 column 21 bridging to column 22 that said compounds are in pharmaceutical compositions used for said method.

12. Thus, it is clear that US`239 anticipates the instant claims, as recited.

Allowable Subject Matter

13. **Claim 10 is objected** to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

14. The following is a statement of reasons for the indication of allowable subject matter: The prior art teaches and discloses processes for compounds of the instant application. For example, albeit US6380239 shows illustratively the process of making dioxoisoindoline compounds, whereas US6765003 shows arylsulfonylpropanoic derivatives, these do have different intermediates and steps in effectuating the resultant compounds.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MLouisa Lao, Ph.D. whose telephone number is 571-272-9930. The examiner can normally be reached on Mondays to Fridays from 8:30am to 5:00pm. If attempts

to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page, can be reached on 571-272-0602. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

`mll 03262007
MLouisa Lao, Ph.D.
Examiner
Art Unit 1621

THURMAN PAGE
SUPERVISORY PATENT EXAMINER
TC1600 GAU 1621